

Amendment to the Claims:

Please amend the claims as follows.

Please cancel claims 46, 51, 54, 91, 92, 95 and 96, without prejudice or disclaimer.

This listing of claims will replace all prior versions, and listing, of claims in the application:

Listing of Claims:

Claim 1 (currently amended): A method for stable transduction of primary T cells of the ~~hematopoietic system~~ and/or T cell ~~hematopoietic~~ stem cells comprising  
contacting the surface of said primary T cell or T cell ~~hematopoietic~~ stem cells at the same time *in vitro* or *ex vivo* with both a lentiviral vector and at least one polypeptide molecule which binds said cell surface by binding to a T cell surface receptor,  
wherein at least about 75% of the T cells are stably transduced after about seven to ten days, or at about 14 days  
and ~~the binding of the cell surface receptor binding molecule to the cell surface receptor does not induce apoptosis of the cell and~~ the binding of the T cell surface receptor binding polypeptide molecule to the T cell surface receptor results in the T cell being more receptive to transduction by the lentiviral vector.

Claim 2 (currently amended): The method of claim 1 further comprising continuous contacting the primary T cells or T cell ~~hematopoietic~~ stem cells *in vitro* or *ex vivo* with the lentiviral vector after the simultaneous contacting of the primary T cells or T cell ~~hematopoietic~~ stem cells with the lentiviral vector and the at least one T cell surface receptor binding polypeptide molecule.

Claim 3 (currently amended): The method of claim 1 further comprising continuous contacting the primary T cells or T cell ~~hematopoietic~~ stem cells *in vitro* or *ex vivo* with the at least one T cell surface binding polypeptide molecule after the simultaneous contacting of the primary T cells or T cell ~~hematopoietic~~ stem cells with the lentiviral vector and the at least one T cell surface receptor binding polypeptide molecule.

Claim 4 (currently amended): The method of claim 1 further comprising continuous contacting the primary T cells or T cell hematopoietic stem cells *in vitro* or *ex vivo* with the lentiviral vector and the at least one T cell surface binding polypeptide molecule after the initial simultaneous contact of the primary T cells or T cell hematopoietic stem cells with the lentivirus vector and the at least one T cell surface receptor binding polypeptide molecule.

Claim 5 (original): The method of claim 1 where said contacting with a lentiviral vector occurs more than once.

Claim 6 (previously presented): The method of claim 1 wherein said lentiviral vector is derived from a human immunodeficiency virus (HIV).

Claim 7 (currently amended): The method of claim 1 wherein said T cell surface receptor binding polypeptide comprises molecule is an antibody, an antigen binding fragment, or a ligand ~~of a cell surface molecule~~.

Claim 8 (original): The method of claim 1 wherein said lentiviral vector comprises at least one cis-acting nucleotide sequence derived from the gag, pol, env, vif, vpr, vpu, tat or rev genes.

Claim 9 (previously presented): The method of claim 8 wherein said cis-acting nucleotide sequence is not expressed or is a fragment or a mutant of the gag, pol, env, vif, vpr, vpu, tat or rev genes.

Claim 10 (previously presented): The method of claim 1 wherein said lentiviral vector is derived from HIV-1 or HIV-2.

Claim 11 (original): The method of claim 1 wherein said lentiviral vector is a pseudotyped vector.

Claim 12 (previously presented): The method of claim 11 wherein said pseudotyped vector comprises the vesicular stomatitis virus G envelope protein.

Claim 13 (previously presented): The method of claim 1 wherein said lentiviral vector is a chimeric vector comprising HIV sequences, wherein optionally the HIV sequences comprise HIV-1 and HIV-2 sequences.

Claim 14 (currently amended): The method of claim 1 wherein said primary T hematopoietic cell is a CD4 positive cell ~~or is a hematopoietic stem cell of a~~ CD4 positive cell.

Claim 15 (currently amended): The method of claim 1 wherein said primary T cell ~~of the hematopoietic system or hematopoietic stem cell is a~~ CD4 positive cell lymphocyte or a precursor thereof.

Claim 16 (currently amended): The method of claim 1 wherein the primary T cell ~~of the hematopoietic system or T hematopoietic stem cell is a~~ CD4 or CD8 positive cell or a CD4 or CD8 positive precursor thereof.

Claim 17 (currently amended): The method of claim 1 wherein said primary T cell ~~of the hematopoietic system or T hematopoietic stem cell is a~~ CD34 positive cell or a CD34 positive precursor thereof.

Claim 18 (currently amended): The method of claim 1 wherein said at least one T cell surface receptor binding polypeptide molecule comprises ~~a molecule selected from the group consisting of~~ an FLT-3 ligand; a TPO ligand; a Kit ligand; antibodies that have the same cell surface binding specificity as FLT-3, TPO, or Kit ligand; a CD3 ligand; a CD28 ligand; a CD25 ligand; a CD71 ligand; a CD69 ligand; or ~~and,~~ antibodies that have the same cell surface binding specificity of CD3, CD25, CD28, CD69 or CD71 ligand.

Claim 19 (currently amended): The method of claim 1 wherein said at least one T cell surface receptor binding polypeptide molecule comprises a ~~molecule selected from the group consisting of~~ FLT-3 ligand, TPO ligand and Kit ligand or a polypeptide having polypeptides or other binding molecules that have the same cell surface binding specificity as FLT-3 ligand, TPO ligand, or Kit ligand.

Claim 20 (currently amended): The method of claim 1 wherein the said ~~primary cell or hematopoietic~~ T stem cell is a dendritic cell or a cell capable of differentiating into a dendritic cell ~~or a precursor thereof~~.

Claim 21 (currently amended): The method of claim 1 wherein said at least one T cell surface receptor binding polypeptide comprises ~~molecule is selected from the group consisting of~~ ~~compositions comprising~~ CD34, CD3, CD28, GM-CSF, IL-4, TNF-alpha; GM-CSF, interferon-alpha; and antibodies or other binding polypeptides molecules that have the same cell surface binding specificity as CD34, CD3, CD28, GM-CSF, IL-4, or ~~or~~ ~~[[and]]~~ TNF-alpha; GM-CSF or interferon-alpha.

Claim 22 (currently amended): The method of claim 1, wherein said at least one T cell receptor surface binding polypeptide comprises ~~molecule is selected from the group consisting of~~ CD3 antibodies or ~~or~~ ~~[[and]]~~ cell surface binding fragments thereof, CD28 antibodies or ~~or~~ ~~[[and]]~~ cell surface binding fragments thereof, combinations of said antibodies or ~~or~~ ~~[[and]]~~ cell surface binding fragments thereof, or polypeptides having and binding molecules that have the same cell surface binding specificities as the antibodies.

Claim 23 (currently amended): The method of claim 22 wherein said at least one T cell surface receptor binding polypeptide molecule comprises (a) a combination of CD3 and CD28 antibodies immobilized on a bead or a surface, or (b) the antibody combination of (a), wherein optionally the bead or surface comprises coated beads.

Claim 24 (currently amended): The method of claim 1, further comprising culturing the ~~primary cells or hematopoietic stem~~ cells under conditions conducive to growth and/or proliferation.

Claim 25 (currently amended): The method of claim 24 wherein said conditions comprise culturing or incubation the ~~primary cells or hematopoietic stem~~ cells with a T cell surface receptor binding polypeptide molecule comprising a cytokine.

Claim 26 (currently amended): The method of claim 25 wherein said cytokine comprises ~~[[is]]~~ interleukin-2.

Claim 27 (original): The method of claim 24 wherein said culturing is for about seven days.

Claim 28 (previously presented): The method of claim 27 wherein said culturing is for about 14 days.

Claim 29 (currently amended): The method of claim 1 wherein said contacting the surface of the ~~primary cells or hematopoietic stem~~ cells at the same time *in vitro* or *ex vivo* with both the lentiviral vector and T cell surface receptor binding polypeptide molecule further comprises (a) contacting the T cell surface with a lentiviral vector for about 24 hours; or, (b) step (a) is repeated at least once.

Claim 30 (previously presented): The method of claim 1 wherein the lentiviral vector is present at an MOI of less than 500, or, the cells are transduced with the vector at a multiplicity of infection (MOI) such that the copies of vector per transduced cell is from about 1 to about 100.

Claims 31 and 32 (canceled)

Claim 33 (original): The method of claim 1 wherein said contacting occurs *ex vivo*.

Claim 34 (currently amended): A method for stable transduction of primary T cells ~~of the hematopoietic system~~ and/or ~~hematopoietic~~ T stem cells comprising

(a) isolating an individual a primary T cell ~~of the hematopoietic system~~ and/or a ~~hematopoietic~~ T stem cell; and

(b) contacting the primary T cell or ~~hematopoietic~~ T stem cell simultaneously *in vitro* or *ex vivo* with a lentiviral vector and an at least one polypeptide molecule that physically interacts with a receptor, ~~marker, or other recognizable moiety~~ on the surface of the primary T cell or ~~hematopoietic~~ T stem cell,

wherein greater than about 75% of the primary T cells or ~~hematopoietic~~ T stem cells are stably transduced after about seven to ten days, or at about 14 days

and ~~the binding of the cell surface receptor binding molecule to the cell surface receptor does not induce apoptosis of the cell and~~ the binding of the cell surface receptor binding polypeptide molecule to the T cell or T stem cell surface receptor results in the cell being more receptive to transduction by the lentiviral vector.

Claim 35 (currently amended): The method of claim 34 further comprising continuous contacting the primary T cells or ~~hematopoietic~~ T stem cells *in vitro* or *ex vivo* with the lentiviral vector after the simultaneous contacting of the primary T cells or T stem cells with the lentiviral vector and the at least one cell surface binding polypeptide molecule.

Claim 36 (currently amended): The method of claim 34 further comprising continuous contacting the primary T cells or ~~hematopoietic~~ T stem cells *in vitro* or *ex vivo* with the at least one cell surface binding polypeptide molecule after the simultaneous contacting of the lentiviral vector and the at least one cell surface binding polypeptide molecule.

Claim 37 (currently amended): The method of claim 34 further comprising continuous contacting the primary T cells or ~~hematopoietic~~ T stem cells *in vitro* or *ex vivo* with the lentiviral vector and the at least one cell surface binding polypeptide molecule after the initial simultaneous contact of the lentivirus vector and the at least one cell surface binding polypeptide molecule.

Claim 38 (previously presented): The method of claim 34 wherein said contacting with a lentiviral vector occurs more than once.

Claim 39 (currently amended): The method of claim 34 wherein said cells are human ~~primary cells of the hematopoietic system and/or human hematopoietic stem~~ cells.

Claim 40 (currently amended): The method of claim 34 wherein said cell surface binding ~~polypeptide comprises molecule~~ is an antibody, an antigen binding fragment, or a ligand ~~on a cell surface molecule~~.

Claim 41 (previously presented): The method of claim 34 wherein said lentiviral vector comprises at least one cis-acting nucleotide sequence derived from the gag, pol, env, vif, vpr, vpu, tat or rev genes.

Claim 42 (previously presented): The method of claim 41, wherein said cis-acting nucleotide sequence is not expressed or is a fragment or a mutant of the gag, pol, env, vif, vpr, vpu, tat or rev genes.

Claim 43 (previously presented): The method of claim 34 wherein said lentiviral vector is an HIV-derived vector.

Claim 44 (previously presented): The method of claim 34 wherein said lentiviral vector is a pseudotyped vector.

Claim 45 (previously presented): The method of claim 44 wherein said pseudotyped vector contains the vesicular stomatitis virus G envelope protein.

Claim 46 (canceled)

Claim 47 (currently amended): The method of claim 34 wherein said primary T cell of the ~~hematopoietic system or hematopoietic stem cell~~ is a CD4 positive cell.

Claim 48 (currently amended): The method of claim 34 wherein said primary T cell of the ~~hematopoietic system or hematopoietic stem cell~~ is a CD4 positive cell lymphocyte or a precursor thereof.

Claim 49 (currently amended): The method of claim 34, [[48]] wherein said cell lymphocyte is a CD4 or CD8 positive cell or a CD4 or CD8 positive precursor thereof.

Claim 50 (currently amended): The method of claim 34 wherein said ~~primary cell of the hematopoietic system or hematopoietic stem cell~~ is a CD34 positive cell or a CD34 positive precursor thereof.

Claim 51 (canceled)

Claim 52 (currently amended): The method of claim 34 wherein said at least one T cell surface receptor binding polypeptide molecule comprises ~~a molecule selected from the group consisting of~~ an FLT-3 ligand; a TPO ligand Kit ligand; antibodies that have the same cell surface binding specificity as FLT-3, TPO, or Kit ligand; CD3 ligand; a CD28 ligand; a CD25 ligand; a CD71 ligand; a CD69 ligand; or [[and,]] antibodies that have are the same cell surface binding specificity of CD3, CD25, CD28, CD69 or CD71 ligand.

Claim 53 (currently amended): The method of claim 34 wherein said at least one T cell surface receptor binding polypeptide molecule comprises ~~a molecule selected from the group consisting of~~ FLT-3 ligand, TPO ligand and Kit ligand or a polypeptide having polypeptides or other binding molecules that have the same cell surface binding specificity as FLT-3 ligand, TPO ligand, or Kit ligand.

Claim 54 (canceled)



Claim 55 (currently amended): The method of claim 34 wherein said at least one T cell surface binding polypeptide comprises ~~molecule is selected from the group of compositions comprising~~ a CD34, a CD3, a CD28, a GM-CSF, an IL-4, a TNF-alpha; a GM-CSF; an interferon-alpha; or ~~[[and]]~~ an antibody or other binding polypeptide ~~molecule~~ that has the same cell surface binding specificity as CD34, CD3, CD28, GM-CSF, IL-4, or ~~[[and]]~~ TNF-alpha, GM-CSF or interferon-alpha.

Claim 56 (currently amended): The method of claim 34 wherein said at least one T cell surface binding polypeptide comprises ~~(a) molecule is selected from the group of~~ CD3 antibodies or ~~[[and]]~~ cell surface binding fragments thereof, CD28 antibodies and cell surface binding fragments thereof, combinations of said antibodies and cell surface binding fragments thereof, or ~~[[and]]~~ binding polypeptides ~~molecules~~ that have the same cell surface binding specificities as the antibodies, or

(b) the T cell surface binding polypeptide of (a), wherein and optionally the least one cell surface binding polypeptide ~~molecule~~ comprises at least two of the cell surface binding polypeptides ~~molecules~~ immobilized on a bead or a surface.

Claim 57 (currently amended): The method of claim 56 wherein said at least one cell surface binding polypeptide ~~molecule~~ comprises a combination of CD3 and CD28 antibodies immobilized on coated beads.

Claim 58 (currently amended): The method of claim 34 further comprising culturing the ~~primary cells or hematopoietic stem~~ cells under conditions conducive to growth and/or proliferation.

Claim 59 (currently amended): The method of claim 58 wherein said conditions comprise further incubation with a cell surface binding polypeptide ~~molecule~~ or a cytokine.

Claim 60 (previously presented): The method of claim 59 wherein said cytokine is interleukin-2.

Claim 61 (previously presented): The method of claim 58 wherein said culturing is for about seven days.

Claim 62 (previously presented): The method of claim 58 wherein said culturing is for about 14 days.

Claim 63 (currently amended): The method of claim 34 wherein said contacting the ~~primary cells or hematopoietic stem~~ cells with a lentiviral vector is for about 24 hours and is optionally repeated at least once.

Claim 64 (previously presented): The method of claim 34 wherein the lentiviral vector is present at an MOI of less than 500, or, the cells are transduced with the vector at a multiplicity of infection (MOI) such that the copies of vector per transduced cell is from about 1 to about 100.

Claim 65 (canceled)

Claim 66 (previously presented): The method of claim 34 wherein said contacting occurs *ex vivo*.

Claim 67 (previously presented): The method of claim 34 wherein said lentiviral vector is derived from a human immunodeficiency virus (HIV), wherein optionally the HIV is HIV-1 or HIV-2.

Claim 68 (previously presented): The method of claim 34 wherein said lentiviral vector is a chimeric vector comprising HIV-1 and HIV-2 sequences.

Claim 69 (previously presented): The method of claim 1 or claim 34, wherein greater than 80%, 85%, 89%, 90%, 91%, 92%, 93%, 94% or 95% of the cells are stably transduced after about 14 days.

Claim 70 (currently amended): The method of claim 34 wherein the individual is infected with (a) a human immunodeficiency virus (HIV), or (b) wherein optionally the HIV is HIV-1 or HIV-2.

Claim 71 (currently amended): The method of claim 70 ~~4 or claim 34~~, wherein (a) the ~~primary cells or hematopoietic stem~~ cells isolated from the HIV-infected individual are pre-stimulated with at least one cell surface binding polypeptide, or (b) the method of step (a) wherein ~~molecule, and optionally the primary cells or hematopoietic stem~~ cells are pre-stimulated with the at least one cell surface binding polypeptide molecule within twenty four (24) hours prior to simultaneously contacting the ~~primary cells or hematopoietic stem~~ cells *in vitro* or *ex vivo* with the lentiviral vector and the at least one cell surface binding polypeptide molecule.

Claims 72 to 82 (canceled)

Claim 83 (previously presented): The method of claim 1 or claim 34, wherein at least 75% of the cells remain stably transduced after about 14 days.

Claim 84 (currently amended): The method of claim 1, the cell surface binding polypeptide further molecule comprises a ~~polypeptide~~, a lipid, a nucleic acid, a carbohydrate or an ion.

Claim 85 (previously presented): The method of claim 1 or claim 34, further comprising introducing the transduced cell into a living subject.

Claim 86 (previously presented): The method of claim 1 or claim 34, further comprising introducing the transduced cell into a tissue or an organ.

Claim 87 (previously presented): The method of claim 1 or claim 34, further comprising introducing the transduced cell into a blastocyst.

Claim 88 (currently amended): A method for stable transduction of primary T cells ~~of the hematopoietic system and/or hematopoietic~~ T stem cells with a lentiviral vector comprising contacting the cell at the same time *in vitro* or *ex vivo* with a lentiviral vector and at least one cell surface receptor binding polypeptide molecule, wherein the lentiviral vector is pseudotyped, wherein the pseudotyping comprises co-transfecting or co-infecting a packaging cell with both the lentiviral vector genetic material and genetic material encoding at least one envelope protein of another virus or a cell surface receptor-binding polypeptide molecule, wherein at least about 75% of the cells are stably transduced after about seven to ten days, or at about 14 days, and optionally at least 75% of the cells remain stably transduced after about 14 days,

~~and the binding of the cell surface receptor binding molecule to the cell surface receptor does not induce apoptosis of the cell and~~ the binding of the cell surface receptor binding polypeptide molecule to the cell surface receptor results in the cell being more receptive to transduction by the lentiviral vector.

Claim 89 (previously presented): The method of claim 88, wherein the lentiviral vector is pseudotyped with a *Rhabdovirus*.

Claim 90 (previously presented): The method of claim 89, wherein the *Rhabdovirus* is a Vesicular Stomatitis Virus envelope G (VSV-G) protein.

Claims 91 and 92 (canceled)

Claim 93 (currently amended): The method of claim 1, claim 34, or claim 88, wherein said at least one cell surface binding polypeptide molecule comprises at least two cell surface binding polypeptides comprising molecules selected from the group consisting of an FLT-3 ligand; a TPO ligand Kit ligand; antibodies that have the same cell surface binding specificity as FLT-3, TPO, or Kit ligand; CD3 ligand; a CD28 ligand; a CD25 ligand; a CD71 ligand; a CD69 ligand; or ~~or~~ [[and,]] antibodies that have are the same cell surface binding specificity of CD3, CD25, CD28, CD69 or CD71 ligand.

Claim 94 (currently amended): The method of claim 1, wherein the at least one cell surface binding polypeptide ~~further molecule~~ comprises a ~~polypeptide~~, a lipid, a nucleic acid, a carbohydrate or an ion.

Claims 95 and 96 (canceled)

Claim 97 (currently amended): The method of claim 93, wherein the at least two cell surface binding polypeptides ~~molecules~~ comprise immobilized  $\alpha$ CD3 and  $\alpha$ CD28.

Claim 98 (currently amended): The method of claim 22, wherein the at least one cell surface binding polypeptide ~~molecule~~ comprises at least two cell surface binding polypeptides ~~molecules~~ immobilized on a bead or a surface.

Claim 99 (previously presented): The method of claim 88, wherein the lentiviral vector is present at an MOI of less than 500, or, the cells are transduced with the vector at a multiplicity of infection (MOI) such that the copies of vector per transduced cell is from about 1 to about 100.